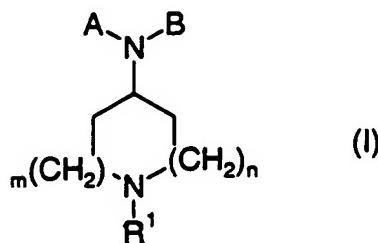


Claims

1. A compound of the formula (I)



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wherein

m is 0 or 1;

n is 1 or 2;

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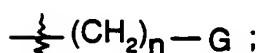
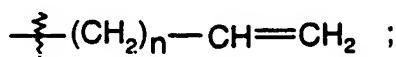
R<sup>1</sup> is selected from

hydrogen;

a branched or straight C<sub>1</sub>-C<sub>6</sub> alkyl;

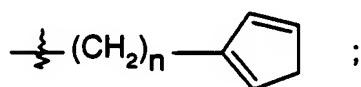
C<sub>3</sub>-C<sub>8</sub> cycloalkyl;

15 C<sub>4</sub>-C<sub>8</sub>(alkyl-cycloalkyl) wherein alkyl is C<sub>1</sub>-C<sub>2</sub> alkyl and cycloalkyl is C<sub>3</sub>-C<sub>6</sub> cycloalkyl;  
benzyl;



where G is a hydroaromatic or a heteroaromatic group having 5 or 6 atoms, and where the

20 heteroatoms are selected from O, S and N; and

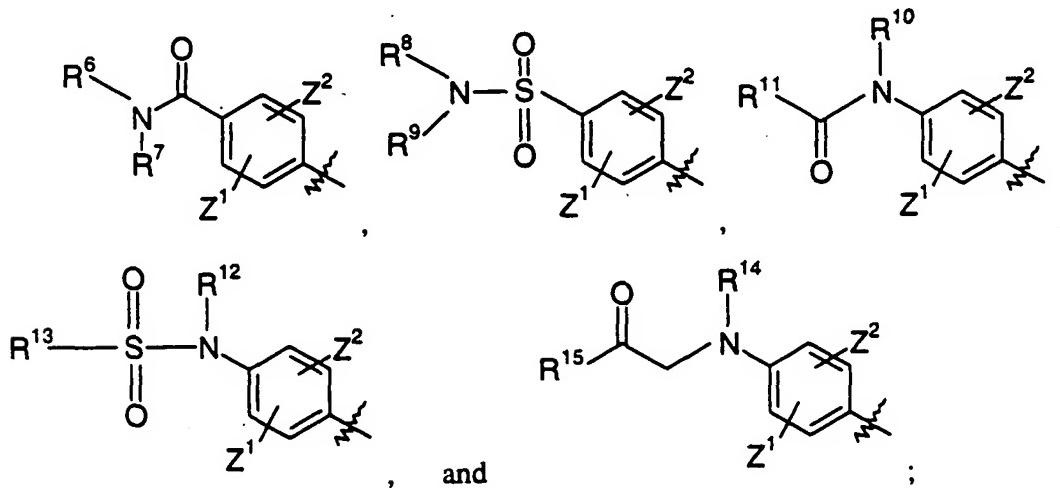


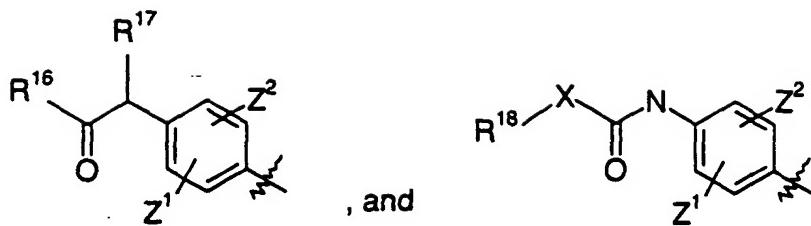
and wherein n = 0 or 1;

$C_6-C_{10}$  aryl; or heteroaryl having from 5 to 10 atoms selected from any of C, S, N and O; wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents independently selected from any of hydrogen,  $CH_3$ ,  $(CH_2)_pCF_3$ , halogen,  $CONR^5R^4$ ,  $COOR^5$ ,  $COR^5$ ,  $(CH_2)_pNR^5R^4$ ,  $(CH_2)_pCH_3(CH_2)_pSOR^5R^4$ ,  $(CH_2)_pSO_2R^5$ , and  $(CH_2)_pSO_2NR^5$ , wherein  $R^4$  and  $R^5$  is each and independently as defined for  $R^1$  above and p is 0, 1 or 2;

$(C_1-C_2$  alkyl)- $(C_6-C_{10}$  aryl); or  $(C_1-C_2$  alkyl)heteroaryl, the heteroaryl moieties having from 5 to 10 atoms selected from any of C, S, N and O, and where the aryl or heteroaryl may optionally and independently be substituted by 1 or 2 substituents independently selected from any of hydrogen,  $CH_3$ ,  $CONR^5R^4$ ,  $COOR^5$ ,  $COR^5$ ,  $(CH_2)_qNR^5R^4$ ,  $(CH_2)_qCH_3(CH_2)_qSOR^5R^4$ ,  $(CH_2)_qSO_2R^5$ ,  $(CH_2)_qSO_2NR^5$ , and  $(CH_2)_qOR^4$ , wherein  $R^4$  and  $R^5$  is each and independently as defined for  $R^1$  above and q is 0, 1 or 2;

15 A is





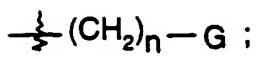
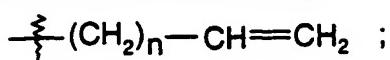
wherein  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$ ,  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$ ,  $R^{16}$ ,  $R^{17}$ , and  $R^{18}$  is each and independently as defined for  $R^1$  above and wherein the phenyl ring of each A substituent may be optionally and independently substituted by 1 or 2 substituents  $Z^1$  and  $Z^2$  which are each and independently selected from hydrogen,  $CH_3$ ,  $(CH_2)_rCF_3$ , halogen,  $CONR^2R^3$ ,  $CO_2R^2$ ,  $COR^2$ ,  $(CH_2)_tNR^2R^3$ ,  $(CH_2)_tCH_3(CH_2)_tSOR^2$ ,  $(CH_2)_tSO_2R^2$  and  $(CH_2)_tSO_2NR^2R^3$  wherein  $R^2$  and  $R^3$  is each and independently as defined for  $R^1$  above and wherein  $r$  is 0, 1, or 2;  $X$  is O, S or  $NR^{19}$  where  $R^{19}$  is as defined for  $R^1$ ,

- 10 B is a substituted or unsubstituted aromatic, heteroaromatic, hydroaromatic or heterohydroaromatic moiety having from 5 to 10 atoms selected from any of C, S, N and O, optionally and independently substituted by 1 or 2 substituents independently selected from hydrogen,  $CH_3$ ,  $(CH_2)_tCF_3$ , halogen,  $(CH_2)_tCONR^5R^4$ ,  $(CH_2)_tNR^5R^4$ ,  $(CH_2)_tCOR^5$ ,  $(CH_2)_tCOOR^5$ ,  $OR^5$ ,  $(CH_2)_tSOR^5$ ,  $(CH_2)_tSO_2R^5$ , and  $(CH_2)_tSO_2NR^5R^4$ , wherein  $R^4$  and  $R^5$  is each and independently as defined for  $R^1$ ; and  $t$  is 0, 1, 2 or 3;

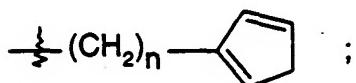
as well as pharmaceutically acceptable salts of the compounds of the formula (I), and isomers, hydrates, isoforms and prodrugs thereof.

2. A compound according to claim 1, wherein

$R^1$  is selected from benzyl;



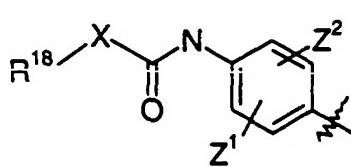
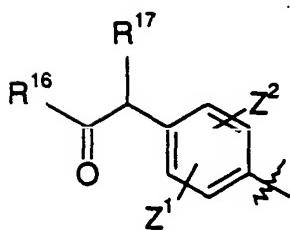
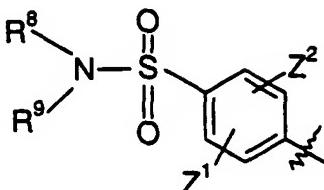
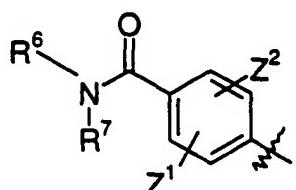
where G is a hydroaromatic or a heteroaromatic group having 5 or 6 atoms, and where the heteroatoms are selected from O, S and N; and



and wherein  $n = 0$  or  $1$ ;

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A is selected from anyone of



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wherein  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{16}$ ,  $R^{17}$  and  $R^{18}$  is each and independently as defined for  $R^1$  above; and  $Z^1$ ,  $Z^2$  and  $X$  is each and independently as defined above;

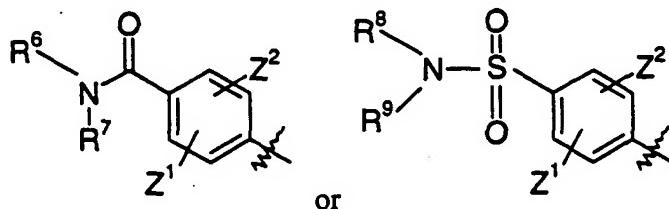
B is selected from phenyl, naphthyl, indolyl, benzofuranyl, dihydrobenzofuranyl,  
20 benzothiophenyl, pyrryl, furanyl, quinolinyl, isoquinolinyl, cyclohexyl, cyclohexenyl,

cyclopentyl, cyclopentenyl, indanyl, indenyl, tetrahydronaphthyl, tetrahydroquinyl,  
 tetrahydroisoquinolinyl, tetrahydrofuranyl, pyrrolidinyl, and indazolinyl,  
 each optionally and independently substituted by 1 or 2 substituents independently  
 selected from hydrogen, CH<sub>3</sub>, CF<sub>3</sub>, halogen, —(CH<sub>2</sub>)<sub>t</sub>CONR<sup>5</sup>R<sup>4</sup>, —(CH<sub>2</sub>)<sub>t</sub>NR<sup>5</sup>R<sup>4</sup>,  
 5 —(CH<sub>2</sub>)<sub>t</sub>COR<sup>5</sup>, —(CH<sub>2</sub>)<sub>t</sub>CO<sub>2</sub>R<sup>5</sup>, and —OR<sup>5</sup>,  
 wherein t is 0 or 1, and wherein R<sup>4</sup> and R<sup>5</sup> are as defined for R<sup>1</sup>.

3. A compound according to claim 2, wherein

10 R<sup>1</sup> is (C<sub>1</sub>-C<sub>2</sub> alkyl)phenyl and hydrogen;

A is



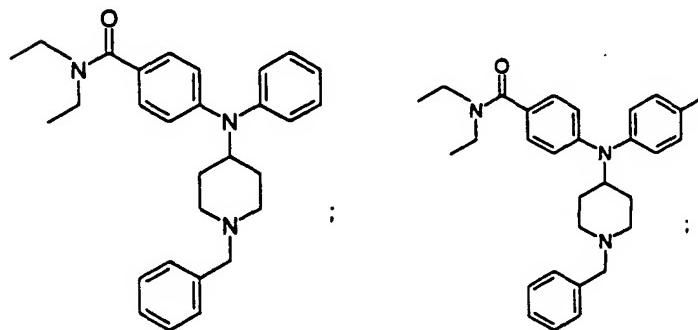
wherein R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, is each an ethylene group; and Z<sup>1</sup> and Z<sup>2</sup>, are as defined above;

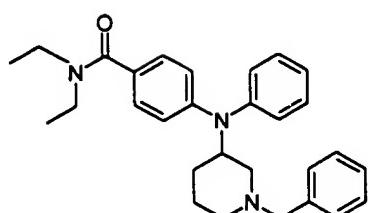
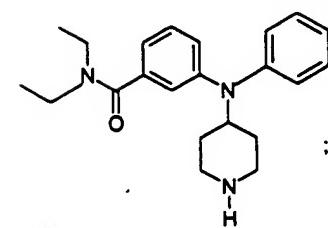
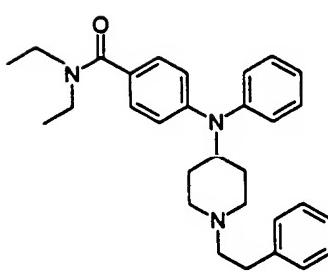
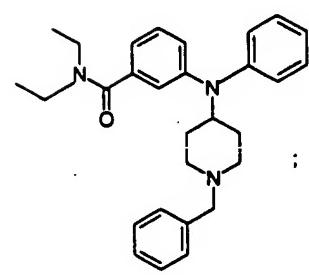
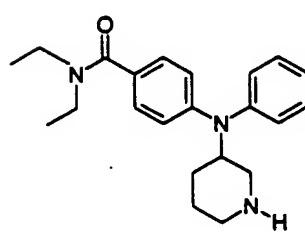
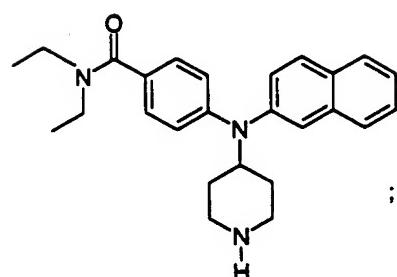
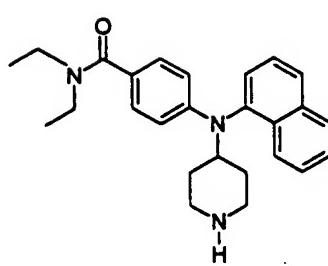
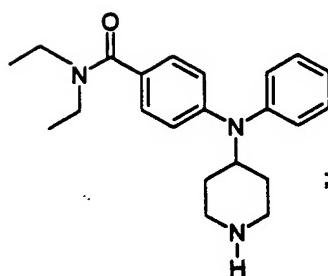
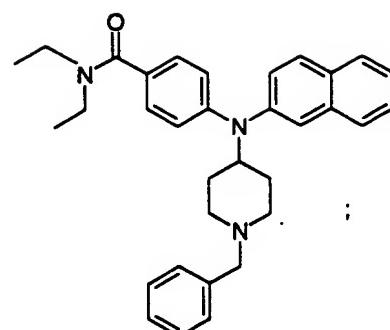
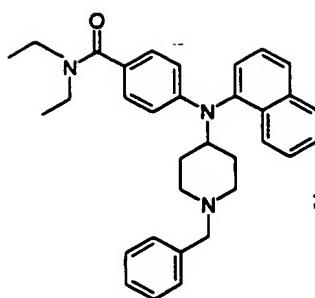
15 B is phenyl or naphthalene; and

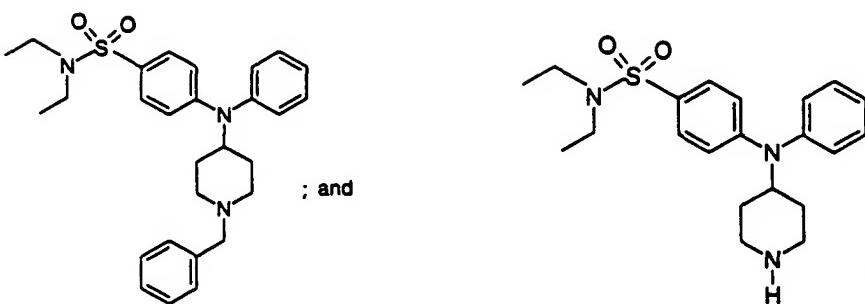
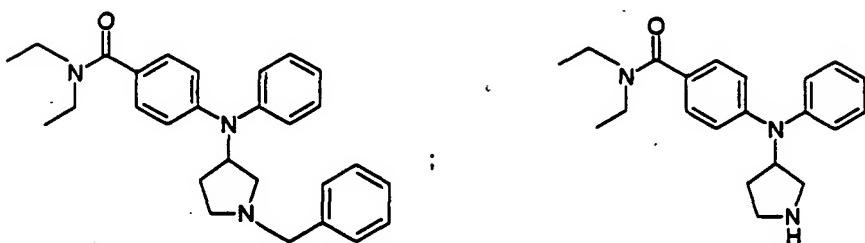
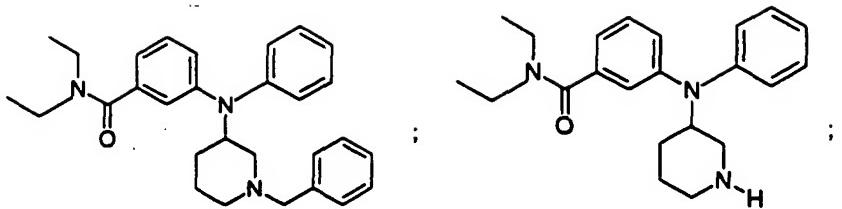
m and n is each 1, or m is 1 and n is 0.

4. A compound according to formula (I) of claim 1, selected from anyone of

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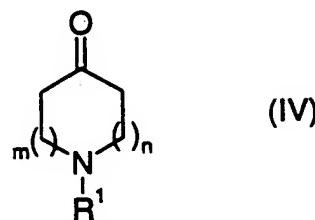


- 10 5. A compound according to any of the preceding claims, in form of its hydrochloride, bitartrate or trifluoroacetate salt.
6. A compound according to any of the previous claims, for use in therapy.
- 15 7. A compound according to claim 6, wherein the therapy is pain management.
8. A compound according to claim 6, wherein the therapy is directed towards gastrointestinal disorders.

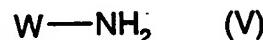
9. A compound according to claim 6, wherein the therapy is directed towards spinal injuries.
- 5 10. A compound according to claim 6, wherein the therapy is directed to disorders of the sympathetic nervous system.
11. Use of a compound according to formula (I) of claim 1 for the manufacture of a medicament for use in the treatment of pain.
- 10 12. Use of a compound according to formula (I) of claim 1 for the manufacture of a medicament for use in the treatment of gastrointestinal disorders.
13. Use of a compound according to formula (I) of claim 1 for the manufacture of a medicament for use in the treatment of spinal injuries.
- 15 14. A compound according to any of claims 1-5, further characterised in that it is isotopically labelled.
- 20 15. Use of a compound according to claim 14 as a diagnostic agent.
16. An isotopically labelled compound of the formula (I) of claim 1.
17. A diagnostic agent comprising a compound of the formula (I) of claim 1.
- 25 18. A pharmaceutical composition comprising a compound of the formula (I) according to claim 1 as an active ingredient, together with a pharmacologically and pharmaceutically acceptable carrier.

19. A process for the preparation of a compound of the formula (I) according to claim 1, whereby

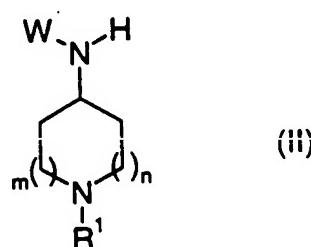
(i) a ketone of the formula (IV)



wherein  $R^1$ ,  $m$  and  $n$  are as defined in formula (I) of claim 1, is subjected to reductive amination with a substituted arylamine of the formula (V)



wherein  $W$  is as defined in formula (I) of claim 1, optionally in the presence of a solvent, giving a compound of the formula (II)



wherein  $R^1$ ,  $m$  and  $n$  are as defined in formula (I) above, and  $W$  is  $A$  or  $B$  as defined in formula (I) above;

20 (ii)  $R^1$  and  $W$  in formula (II), are optionally modified after or during preparation of (II) from (IV) and (V);

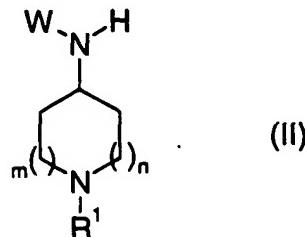
(iii) the compound of the formula (II) achieved in step (i), is subjected to an arylation reaction, by reaction with an arylating agent of the formula (III)



wherein W is A or B as defined in formula (I) above, and Z is a suitable substituent, optionally in the presence of a catalyst, giving a compound of the formula (I) of claim 1; and

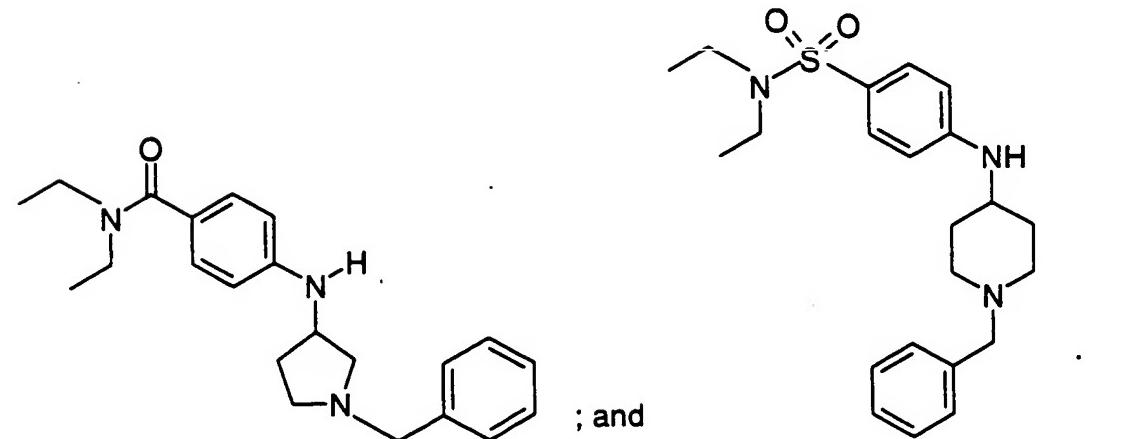
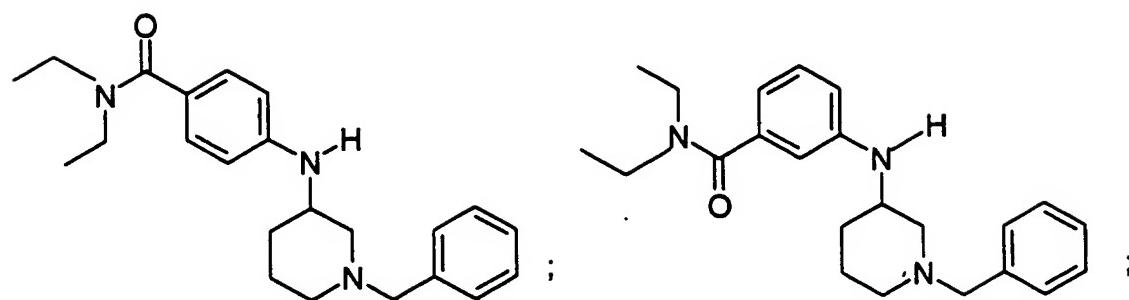
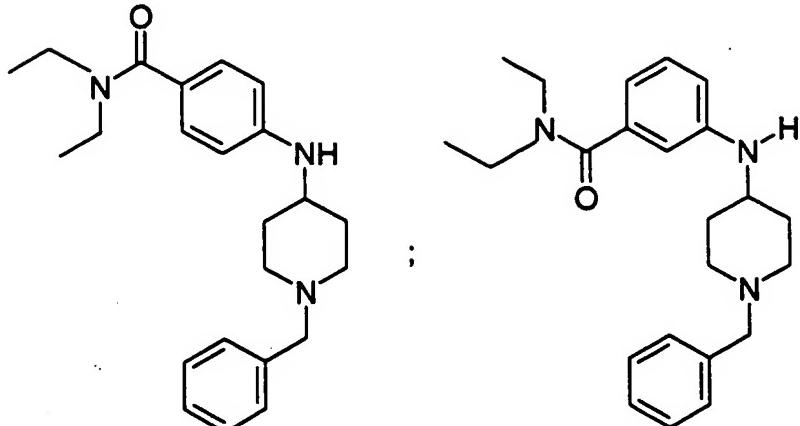
10      (iv) R<sup>1</sup>, and the substituents on A and B, are optionally further modified.

20.      A compound of the formula



wherein R<sup>1</sup>, m and n are as defined in formula (I) of claim 1, and W is as defined for A or B in formula (I) of claim 1.

21. A compound of the formula (II) of claim 17, selected from any of



22. A method for the treatment of pain, whereby an effective amount of a compound of the formula (I) according to claim 1 is administered to a subject in need of pain management.

5 23. A method for the treatment of gastrointestinal disorders, whereby an effective amount of a compound of the formula (I) according to claim 1, is administered to a subject suffering from said gastrointestinal disorder.

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24. A method for the treatment of spinal injuries, whereby an effective amount of a compound of the formula (I) according to claim 1, is administered to a subject suffering from said spinal injury.

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